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Aortic stiffness index and diurnal variability (dipper/non-dipper) in hypertensive patients

Aortic stiffness and hypertension

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Abstract

Aim: Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients. In this study, we aimed to evaluate how aortic elasticity parameters [aortic distensibility (AD), aortic stiffness index (ASI), aortic strain (AS)] is affected by the diurnal rhythm of the blood pressure in hypertensive and normotensive individuals without a known cardiovascular disease. Material and Method: In this cross-sectional study, 58 hypertensive and 60 normotensive patients without known cardiovascular disease were enrolled. Ambulatory blood pressure monitoring was performed on hypertensive patients, and transthoracic echocardiography was performed on all study participants. The AD, ASI, and AS were compared between controls, dippers, and non-dippers. Results: In our study, the highest "aortic stiffness index" value was detected in reverse dippers group followed by non-dippers group, dippers group, and control group with regard to age. Also, aortic strain and aortic distensibility values were highest in control group, respectively dippers group, non-dippers group and reverse dippers group. Discussion: We determine there is a relation with the diurnal rhythm of blood pressure and aortic stiffness parameters.

Keywords

Aortic Stiffness; Aortic Elasticity; Dipping Hypertension; Non-Dipping Hypertension; Nocturnal Blood Pressure

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Introduction

Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality. It occurs as a result of aging, smoking, hypercholesterolemia, diabetes mellitus and hypertension [1,2]. Increased aortic stiffness or decreased distensibility is indicative of the extensive involvement of atherosclerotic vascular system [3]. It has a decisive importance for vascular disorders such as renal disease, stroke, heart failure and myocardial infarction [4,5].

Ambulatory blood pressure monitoring (ABPM) is a frequently used method to diagnose or follow up hypertension. It is considered to be useful for patients with suspected white-coat hypertension, in elderly with resistant hypertension having symptoms related to hypotension due to antihypertensive drugs and in patients who are believed to have important changes in nocturnal blood pressure.

Normal population studies revealed a nocturnal decrease in blood pressure (BP) in adults. If the average systolic BP (SBP) and diastolic BP (DBP) difference between waking and sleeping is 10–20%, then it is considered as dipping pattern; if the difference is <%10 then it is considered as non-dipping pattern and also nocturnal blood pressure is high during the day it is considered as reverse-dipping pattern. Patients having a difference >%20 were considered to have an extreme-dipping pattern.The underlying pathogenetic mechanisms of the non-dipping pattern are not fully understood. There are multiple possible underlying pathophysiological mechanisms in the impaired BP decrease at night. Abnormal neurohormonal regulation, increased dietary sodium intake, sedentary life and smoking of tobacco have been implicated in the blunted circadian rhythm of BP [6]. Certain diseases such as diabetes and chronic renal diseases also affect the circadian BP rhythm.

The aim of this study was to evaluate how aortic elasticity is affected by the diurnal rhythm of BP in hypertensive individuals without a known cardiovascular disease.

Material and Method

Study Design and Patient Population: In this study, 58 hypertensive patients who were previously diagnosed with essential hypertension and followed with medical therapy and 60 controls without hypertension were included. Patients with known or suspected coronary artery disease (CAD), reduced ejection fraction (EF) (<%60), more than mild valvular stenosis/regurgitation, heart failure, cardiomyopathy, prosthetic heart valve, secondary hypertension, renal failure, history of cerebrovascular accident, congenital or acquired aortic diseases, aortic aneurysm, history of cardiovascular or aortic surgery, connective tissue disorders, low-quality echocardiographic and ultrasonographic images, conduction abnormalities, and atrial fibrillation on the electrocardiogram (ECG) were excluded. BP measurements were performed a week apart, at sitting position and after the rest for 5-10 minutes. Patients with a blood pressure of <140/90 were considered normotensive. ABPM was applied to the hypertensive group. Hypertensive patients were taking angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), thiazide diuretics group, and calcium channel blockers as a monotherapy or combination therapy.

Ambulatory Blood Pressure Recording: The recorder was programmed to take BP measurements every 15 minutes during the daytime and every 30 minutes during the nighttime. The daytime period was defined as the interval between 6 AM and 12 PM and the nighttime period as between 12 PM and 6 AM. The patients were instructed to attend their usual day-to-day activities, but to keep still and relax their arms at the times of measurements. For the following conditions, the values were not taken into consideration: Systolic BP (SBP) >270 mmHg and <70 mmHg, for diastolic BP (DBP) >150 mmHg and <40 mmHg values; Equal measurements of SBP's and DBP's; >30 mmHg differences between the following 2 measurements of SBP's or DBP's. If the acceptable BP values were over 14 at daytime and over 7 at night, records were considered adequate.

Echocardiographic Examination: The echocardiographic examinations were obtained using "General Electric Vivid 7" with a multifrequency transducer (2.5–3.5 MHz) equipped with tissue Doppler imaging (TDI) technology (Vingmed Ultrasound, GE, Horten, Norway). All echocardiographic measurements were performed in five consecutive cycles, and their average was used for the calculations. Two-dimensional and standard M-Mode measurements were performed according to the American Society of Echocardiography (ASE) recommendations [7]. The EF, end-diastolic volume, and end-systolic volume were analyzed by the Simpson method and Teichholz method.

For the calculation of aortic stiffness, the diameter of the ascending aorta was measured from the same view on the M-mode tracing at a level of 3 cm above the aortic valve. The systolic aortic diameter (AoS) was measured at the maximal anterior motion of the aorta, whereas the diastolic aortic diameter (AoD) was measured at the peak of the QRS complex on the simultaneously recorded ECG. Five consecutive measurements were performed, and their mean was calculated. At this time, brachial blood pressure was measured.

Assessment of Aortic Stiffness: Aortic elasticity was calculated according to the following three formulas:

''Aortic strain'' (AS) = (AoS-AoD)/AoDx100,

"Aortic distensibility" (AD) = (2×Aortic strain/100)/(SBP-DBP) (10^{-3} cm2.dyn^{-1})

"Aortic stiffness index" (ASI)= ln(SBP/DBP)/(AORTIC strain/100)

AoD = aortic root end-diastolic diameter, AoS =aortic root end-systolic diameter

Statistical analysis were performed with SPSS 18.0 (PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.) software. Kolmogorov-Smirnov test was used to evaluate normal distribution. Continuous variables were expressed as mean ± SD or median; categorical variables were defined as numbers and percentages. Student's t-test was used to compare continuous variables. Differences in the distribution of categorical variables were assessed by chi-square analysis. One-way analysis of variance (ANOVA) was used to analyze the intragroup comparisons. A p-value <0.05 was considered significant. Post-hoc multiple comparisons were made using Bonferroni correction.

Results

We enrolled 118 participants, and 23 (%39,65) were in the dippers group, 28 (%48,27) in the non-dippers group, 7 (%12,01) in the revers-dippers group, and 60 in the control group. Mean age of the hypertensive patients were 47,6 ±8,63 years and mean age of the control group were 48,5 ±7,0 years. Mean age was 44,5 ±9,7 years in dippers group, 50,1 ±7,7 in the non-dippers group, 47,5±5,7 in reverse dippers group. The majority of the participants were women (%69,49). In the dippers group there were 14 women and 9 men, in the non-dippers group there were 22 women and 6 men, in reverse dippers group there were 4 women and 3 men. The mean ambulatory systolic and diastolic blood pressure of hypertensive patients was 127,1±14,3/71,3±10,5 mmHg under drug treatment. It was 125,0±11,3/71,3±10,2 mmHg on dippers group, 126,3±14,7/69,5±9,5 mmHg on non dippers group, 134,0±20,0/78,5±13,7 on reverse dippers group. The mean clinical blood pressure of normotensive patients was 122,5±17,2/78,8±13,0 mmHg. Mean creatinine values of the control group were found to be lower than those of patient group although the patients who had impaired renal function tests were excluded, and there was no statistically significant difference between the groups in the subgroup analysis. The demographic and clinical characteristics of the patients are summarized in Table 1.

There was a significant difference between dippers group, non-dippers group, reverse group, and control group in terms of AS, AD, ASI. AS and AD was lowest in reverse dippers group, but ASI was highest in reverse dippers group (Table 2).

AS was significantly higher in control group compared to non-dippers, reverse dippers groups (p<0,01, p<0,01) respectively. There was no significant difference between the control and the dippers groups in terms of AS and ASI (p:0,87, p:0,23). AD was higher in control group than the dippers group, non dippers group, reverse dippers group (p<0,01, p<0,01, p<0,01) respectively. AS and AD were significantly higher in dippers group compared to non-dippers and reverse dippers group (p<0,01, p<0,01, p<0,01, p<0,01) respectively. ASI was significantly lower in dippers group compared to non-dippers and reverse group (p<0,01, p<0,01) respectively. There was no significant difference between non-dippers and reverse dippers groups in terms of AS and ASI (p=0,56, p=0,54). The AD was significantly higher in the non-dippers group than the reverse dippers group (p<0,01) (Table 3).

Table 1. Clinical and demographic characteristics of patients

	Control (n:60)	Dippers(n:23)	Non dippers(28)	Revers dippers(n:7)	P value
Age (years)	48,5 ±7,0	44,5 ±9,7	50,1 ±7,7	47,5 ±5,7	0,077
Sex (n)	W:41, M:19	W:14, M:9	W:22, M:6	W:4, M:3	0,505
DM (n,%)	12 (%20)	4(%17,3)	5(%17,8)	1(%14,2)	0,979
Smoke (n,%)	14(%23,3)	4(%17,3)	4(%14,2)	3(%42,8)	0,376
Height (cm)	162,1 ±8,9	163,6 ±7,8	162,5 ± 8,9	159,1 ±8,3	0,650
Weight (kg)	77 ±13,6	81,2 ±16,0	80,8 ±13,4	88,5 ±16,7	0,165
Waist circumference (cm)	98,2 ±12,3	102,3 ±13,8	102,1 ±12,8	110,5 ±14,0	0,073
SBP (mmHg)	122,5 ±17,2	125 ±11,3	126,3 ±14,7	134,0 ±20,7	0,290
DBP (mmHg)	78,8 ±13,0	71,3 ±10,2	69,5 ±9,5	78,5 ±13,7	0,001
LDL (mg/dl)	118,9 ±34,2	129,7 ±30,0	128 ±34,2	123,3 ±34,2	0,488
HDL (mg/dl)	54,7 ±16,7	52,3 ±9,3	49,9 ±11,6	50,7 ±8,9	0,480
TG (mg/dl)	125,1 ±65,0	183,3 ±109,9	160,8 ±56,7	138,7 ±55,5	0,010
Blood Glucose (mg/dl)	92,4 ±26,7	92 ±9,7	121 ±67,6	121,0 ±40,0	0,006
Creatinin (mg/dl)	0,74 ±0,16	0,85 ±0,17	0,83 ±0,23	0,84 ±0,20	0,035*
HT Time (years)	-	3,04	3,86	2,71	0,63

* In subgroup analysis there was no significant difference between creatinine levels.
# DM: Diabetes mellitus, SBP: systolic blood pressure, DBP: diastolic blood pressure, LDL: low density lipoprotein, HDL: high density lipoprotein, TG: triglycerides, HT: hypertension

Table 2. Comparison of aortic elasticity between controls, dippers, non-dippers and reverse dippers

	Control (n:60)	Dippers (n:23)	Non dippers (n:28)	Reverse dippers (n:7)	P value
AS	12,1 ±2,3	11,6 ±2,9	6,0 ±2,4	4,6 ±2,2	<0,001
ASI	3,6 ±1,0	5,2 ±1,8	11,7 ±5,9	13,5 ±5,7	<0,001
AD	6,0 ±1,9	4,3 ±1,1	2,1 ±0,9	1,7 ±0,9	<0,001

* AS: aortic strain, ASI: aortic stiffness index, AD: aortic distensibility

Discussion

In our study, the aortic elasticity parameters AS and AD were significantly lower, and ASI was higher in the non-dippers group than dippers group. Also, ASI was higher and AS, AD was lower in reverse dipper group than other 3 groups: normal subjects, the dippers, and the non-dippers group.

There is a clear, albeit complex, relationship between great artery stiffness and atherosclerosis. Arterial stiffness and atherosclerosis usually co-exist, and some studies have described a correlation between atherosclerotic burden and aortic stiffness. In a series of clinical studies, increased arterial stiffness was shown in patients with CAD compared to the ones without CAD [8-11].

Arterial stiffness is a predictor of future cardiovascular and coronary events [12]. Arterial stiffness was shown to increase with age in a group of patients without cardiovascular risk factors [13]. After eliminating aging effects and other risk factors, increased arterial stiffness is an indicator of CAD, cerebrovascular and peripheral artery atherosclerosis [14,15]. Increasing arterial stiffness with advancing age, has been associated with a rise in SBP and pulse pressure (PP). An increase in SBP along with a decrease in DBP arising from the increase in PP—an indicator of the impaired elastic parameters of aorta—may lead to an elevation in left ventricle afterload and thereby impairing coronary perfusion [16,17]. Elastic parameters of aorta were shown to be a strong and independent risk factor for recurrent

Table 3. Comparison of aortic elasticity parameters between subgroups

		Co-Di	Co-NonDi	Co-RDi	Di-Non-Di	Di-RDi	Non-Di-RDi
AS	Mean difffe-rence	0,46	6,09	7,44	5,62	6,97	1,35
	p	0,87	<0,001	<0,001	<0.001	<0.001	0,56
AD	Mean difffe-rence	1,61	3,81	4,27	2,19	2,65	0,45
	p	<0,001	<0,001	<0,001	<0,001	0,001	<0,001
ASI	Mean difffe-rence	-1,53	-8,05	-9,92	-6,52	-8,38	-1,86
	p	0,23	<0,001	<0,001	<0,001	<0,001	0,54

*Co-Di: Control group and dippers group. Co-NonDi: Control group and non dippers group. Co-RDi: Control group and revers dippers group. Di-RDi: Dippers group and Revers dippers group. NonDi-RDi: Non dippers and revers dippers group
AS: aortic strain, ASI: aortic stiffness index, AD: aortic distensibility

acute coronary events in patients with CAD [18]. Great artery stiffness was reported to be the major indicator of exercise-related myocardial ischemia in patients with moderate CAD [19]. A nocturnal decrease in BP as a characteristic of diurnal BP alteration was first put forward by Hill in 1898. Subsequently, less than 10% decrease in nocturnal BP was found to be related to left ventricle hypertrophy, cerebrovascular injury and cardiovascular events [20-22]. Kazuomi et al. detected a high occurrence of stroke in patients having reverse dipping and extreme dipping compared to the patients having dipping and non-dipping patterns. An extreme decrease in nocturnal SBP was proposed to cause silent cerebral infarcts through leading to cerebral hypoxia in patients with "extreme dippers" pattern [23].

Physiological reduction in the night BP decreases with age. The possible reasons for this are suggested to be aging, decrease in great vessel distensibility values due to atherosclerosis, and dominance of sympathetic system-related vasoconstriction on parasympathetic system-related vasodilation as the result of the impairment in autonomic nervous system [24].

In accordance with our results, Bitigen et al. have also shown that there is a relation between diurnal BP pattern and aortic elastic properties. They reported that the highest ASI value was found in reverse dippers patients followed by non-dippers patients and the lowest in dippers patients. The ASI value of reverse dippers and non-dippers was higher than in the dippers group [25].

Our study has some limitations. One of the main limitations of this study is the small sample size. Further large-scale studies will be required to validate our results. Secondly, our study was a cross-sectional study so it couldn't help to determine cause and effect. Another limitation is that the drug treatments used in the hypertension group are not homogeneous. It may have affected the diurnal rhythm of blood pressure. It may not be appropriate to establish a one-way causal link between two determinants; as nocturnal blood pressure decrease and arterial stiffness, because of they were influenced by many factors. In our study, the patients who had known cardiovascular diseases, which could influence the aortic elasticity properties, were excluded.

Conclusion

We detected a relationship between two independent determinants of cardiovascular and cerebrovascular events development; "aortic stiffness parameters" and "inadequate nocturnal blood pressure decrease". According to this relationship, aortic stiffness was observed highest in reverse dippers group followed by non-dippers, dippers and control groups. Aortic stiffness may be one of the early stage findings of atherosclerosis. Mortality and morbidity may be reduced through detection and proper treatment of increased aortic stiffness in the early period in hypertensive patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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